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Dear Francis,

Please excuse the delay in answering your letter of July 16th. I was hoping we could get further in our characterization of the SV40 "mini-chromosomes" before responding.

Unfortunately things are still in a rather unsatisfactory state especially with trying to answer any of the questions you and Roger raised. What we think (I'd like to see additional experiments to strengthen these thoughts) we know is that virtually all of the SV40 DNA in the nucleus of an infected cell is in the form of a 45S nucleoprotein complex (the free DNA derived from the 45S complex by SDS treatment sediments at 21S). Microscopically this complex appears predominantly (>80%) as a "doughnut"( ) and varying amounts of "horseshoes"( ). The contour length of the doughnut is about 0.1 that of the free circular DNA and the thickness of the fiber of the doughnut is about 100A; the amount of DNA "exposed" in the "horseshoe" is not more than 5% of the total DNA of a ring. These rings when incubated in 1 M Na^+ at 37° for 60' lose virtually all of the bound protein as they now sediment at about 22S (we have the feeling there may still be some protein bound as the "dissociated" molecules always sediment a bit faster than the free DNA marker). Jack Griffith has looked at the rings a minute or two after exposure to high salt and he's certain the rings begin to unfold so that the rings become larger and the compact fibre even begins to acquire a "ribbon" appearance. Still later the free DNA strands begins to be released and still later they begin to look like phage particles that are spilling their DNA. (Please pardon the unquantitative description at this stage). According to Peres I^{125}-iodenation of the total protein in the complex yields three labeled bands on SDS gels: their MW's are 15 K, 12 K and 10 K and they correspond in their mobility to the minor components found in the intact virion which Lionel Crawford has characterized as

cellular histones. Perez tells me that the ratio of protein to DNA is near one since glutaraldehyde-fixed complex bands in CsCl at a density expected for a 1:1 protein nucleic acid complex (this is another experiment that needs proper redoing).

As you can see from what I've said, there are presently no answers to the questions you asked. Hopefully this fall one of the new fellows will look at these nucleoportein complexes, clean up some of the uncertainties and get on with a more detailed analysis of their structure; particularly, whether specific regions of the DNA are uncovered.

With best regards to Roger, Sydney, Mark and the rest of the MRC crowd.

Sincerely yours,

PB:af